Vitamin C treatment promotes mesenchymal stem cell sheet formation and tissue regeneration by elevating telomerase activity.

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Public Summary:
With rapid progress in stem cell research, stem cell therapies have become promising therapeutic approaches in clinics. Cell-based regenerative medicine has recently been extensively investigated. However, in past decades, tissue fabrication techniques in regenerative medicine largely relied on scaffold-based approaches. Numerous challenges existed in fabricating functional tissue-engineered organs. These barriers include insufficient cell migration into and retention within scaffolds, host inflammatory reactions, limited capabilities to generate microscale vascularization for mass transport, different rates of cell proliferation compared with scaffold degradation, and the inability to generate functional tissues with the architectural complexity of native tissues because of scaffold-based methods. It has been speculated that the use of continuous cell sheets, with the preservation of cellular junctions, endogenous extracellular matrix (ECM), and mimicking cellular microenvironments in terms of various mechanical, chemical, and biological properties, may be beneficial for cell transplantation. Cell sheet engineering has been developed as an alternative approach to improve mesenchymal stem cell-mediated tissue regeneration. In this study, we found that vitamin C (Vc) was capable of inducing telomerase activity in periodontal ligament stem cells (PDLSCs), leading to the up-regulated expression of extracellular matrix type I collagen, fibronectin, and integrin β1, stem cell markers Oct4, Sox2, and Nanog as well as osteogenic markers RUNX2, ALP, OCN. Under Vc treatment, PDLSCs can form cell sheet structures because of increased cell matrix production. Interestingly, PDLSC sheets demonstrated a significant improvement in tissue regeneration compared with untreated control dissociated PDLSCs and offered an effective treatment for periodontal defects in a swine model. In addition, bone marrow mesenchymal stem cell sheets and umbilical cord mesenchymal stem cell sheets were also well constructed using this method. The development of Vc-mediated mesenchymal stem cell sheets may provide an easy and practical approach for cell-based tissue regeneration.

Scientific Abstract:
Cell sheet engineering has been developed as an alternative approach to improve mesenchymal stem cell-mediated tissue regeneration. In this study, we found that vitamin C (Vc) was capable of inducing telomerase activity in periodontal ligament stem cells (PDLSCs), leading to the up-regulated expression of extracellular matrix type I collagen, fibronectin, and integrin beta1, stem cell markers Oct4, Sox2, and Nanog as well as osteogenic markers RUNX2, ALP, OCN. Under Vc treatment, PDLSCs can form cell sheet structures because of increased cell matrix production. Interestingly, PDLSC sheets demonstrated a significant improvement in tissue regeneration compared with untreated control dissociated PDLSCs and offered an effective treatment for periodontal defects in a swine model. In addition, bone marrow mesenchymal stem cell sheets and umbilical cord mesenchymal stem cell sheets were also well constructed using this method. The development of Vc-mediated mesenchymal stem cell sheets may provide an easy and practical approach for cell-based tissue regeneration. J. Cell. Physiol. (c) 2011 Wiley Periodicals, Inc.